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(54) Title: *LISTERIA*-BASED EPHA2 IMMUNOGENIC COMPOSITIONS

(57) Abstract: The present invention provides nucleic acid constructs comprising a nucleotide sequence encoding an EphA2 antigenic peptide and *Listeria* comprising such constructs. In particular, the present invention provides *Listeria* engineered to express a plurality of EphA2 antigenic peptides and immunogenic compositions comprising such *Listeria*. The invention encompasses, *inter alia*, the use of the immunogenic compositions for eliciting an immune response against an EphA2-expressing cell, as well as for the treatment, management and/or prevention of a hyperproliferative disorder and/or a disease involving aberrant angiogenesis.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/05512

A. CLASSIFICATION OF SUBJECT MATTER

IPC: **A61K 39/00**(2006.01);**39/02**(2006.01);**C12P 1/00**(2006.01);**C07H 21/02**(2006.01);**21/04**(2006.01)

USPC: 424/184.1,234.1,235.1;435/41;536/23.1,23.7

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/184.1,234.1,235.1;435/41;536/23.1,23.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

BIOSIS, SCISEARCH, ARIGCOLA, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/037233 A2 (KINCH ET AL) 28 April 2005 (28.04.2005), see the entire document.	1-14, 17-18 and 36
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A		15-16, 19-35 and 37-38
A	MOODY ET AL, Recombinant Listeria monocytogenes-based immunotherapy targeting the Receptor Tyrosine Kinase EphA2, Proc Amer Assoc Cancer Res, Volume 45, 2004, Abstract only. See the Abstract.	1-38



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:		"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/05512

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-38

- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US07/05512

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Claims 1-38 are drawn to a nucleic acid comprising an act promoter operatively linked to a nucleotide sequence encoding an EphA2 antigenic peptide, a Listeria bacterium comprising the nucleic acid molecule and a composition comprising the nucleic acid molecule.

Claims 39-63 are drawn to a method of eliciting an immune response against an EphA2-expressing cell in a subject.

Claims 64-96 are drawn to a method of preventing or treating a hyperproliferative disorder of EphA2-expressing cells in a human subject.

Claims 97-102 are drawn to be a method of treating a human subject having a disease involving aberrant angiogenesis.

The special technical feature linking Groups I-IV appears to be the EphA2 nucleic acid molecule.

However, Robert Sanders, media Relations, UC Berkeley Press Release, September 29, 2004 teach genetically engineered Listeria and inserted cancer antigens (page 1). Sanders also teach doubly attenuated Listeria strains as a platform for various cancer vaccines (page 2). Sanders teaches that MedImmune, Inc. developed a Listeria-based vaccine targeting the large number of tumors, including breast, prostate and melanoma, that overexpress the antigen Eph2 (page 3). -

The special technical feature of Group I is considered to be a nucleic acid comprising an act promoter operatively linked to a nucleotide sequence encoding an EphA2 antigenic peptide, a Listeria bacterium comprising the nucleic acid molecule and a composition comprising the nucleic acid molecule.

The special technical feature of Group II is considered to be a method of eliciting an immune response against an EphA2-expressing cell in a subject.

The special technical feature of Group III is considered to be a method of preventing or treating a hyperproliferative disorder of EphA2-expressing cells in a human subject.

The special technical feature of Group IV is considered to be a method of treating a human subject having a disease involving aberrant angiogenesis.